The information provided herein is considered JRD, LLC trade secrets, commercial or financial information that JRD, LLC customarily holds close and treats as confidential. The information is being provided under the assurance that the U.S. Department of Health and Human Services and all of its agencies, including the Assistant Secretary for Preparedness and Response, Biomedical Advanced Research and Development Authority, will maintain the confidentiality of the information under the Trade Secrets Act, Procurement Integrity Act, other applicable statutes, regulations, rules, case law contractual provisions, protective orders or otherwise and as such, the information provided herein is exempt from disclosure under Exemption 4 of the Freedom of Information Act ("FOIA").

AMENDMENT OF OTHER TRANSACTION AGREEMENT (OTA)

OTHER TRANSACTION FOR ADVANCED RESEARCH (OTAR)

Agreement Number HHSO100201700018C
Effective Date of Agreement: August 15, 2017

BETWEEN

JANSSEN RESEARCH & DEVELOPMENT LLC
920 ROUTE 202
RARITAN, NJ 08869, USA

AND

THE UNITED STATES OF AMERICA
DEPARTMENT OF HEALTH AND HUMAN SERVICES
BIOMEDICAL ADVANCED RESEARCH AND DEVELOPMENT AUTHORITY
O'NEILL HOUSE OFFICE BUILDING
WASHINGTON, DC 20515

CONCERNING

INFLUENZA PORTFOLIO AND OTHER EMERGING PATHOGENS DEVELOPMENT CANDIDATES

Amendment No. 0008

Effective Date of Modification: Upon Last Signature in Section III

Total Amount of the Agreement is increased by (b) (4) for addition COVID (b) (4) (b) (4) cost share adjustment from $715,837,436 to (b) (4) (Includes Recipient and Government Funding).

Government Share of Total Amount of the Agreement is increased by $498,768,315 from $520,433,037 to $1,019,201,353.

Recipient Share of Total Amount of the Agreement is increased by (b) (4) for scope increase (b) (4) cost share adjustment from (b) (4) to (b) (4)

Current Government commitment: with the scope/cost estimate adjustment to Work Packages ("WP") 6.1 - 6.7 and the addition and authorization of WPs 6.8 – 6.10 and 6.13 – 6.16, the total Funds Obligated is increased by $456,237,081 from $233,288,786 to $689,525,867.

Current Recipient commitment: with the scope/cost estimate adjustment to WPs 6.1 - 6.7, the addition and authorization of WPs 6.8 – 6.10 and 6.13 – 6.16 of (b) (4), and the (b) (4) (b) (4) the total Recipient Funds Obligated is increased by (b) (4) from (b) (4) to (b) (4)

Authority: Section 319L(C)(5) of the Public Health Service Act, 42 USC 247d-7e(C)(5).

Line of Accounting and Appropriation:

(b) (4)

WP 6.1 – 6.10, and 6.13 – 6.16	COVID-19 - Vaccines discovery thru Phase 3 Trial, excluding WPs 6.11 and 6.12.	OS256464 OS256544	199COV1 199COV1	25103 25103	$456,048,121 $ 188,960 **$456,237,081**	Added with this modification
(b) (4)						
Total					**$689,525,867**	**Changed**

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I. AMENDMENT PURPOSE

This Amendment seeks to utilize Recipient's expertise to perform research and development for vaccine and therapeutic candidates for the current COVID-19 pandemic and declared public health emergency.

By the Parties' mutual agreement and within the existing Agreement's general scope, this Amendment No. 0008 bilaterally:

i. replenishes funding (b) (4) to the COVID-19 vaccine efforts added to Amendment 0006;

ii. incorporates the scope of work previously added via Amendment 0006 for Pre-clinical thru Clinical Phase 1 Study, WPs 6.1 - 6.7, which will be removed from Amendment 0006 and will be added to this Amendment 0008;

iii. adjusted Work Packages 6.1 - 6.7 to reflect an updated scope and budget;

iv. exercises Work Package 6.7;

v. adds Work Packages 6.8 - 6.16;

vi. updates the Statement of Work (Exhibit-A) to reflect COVID-19 Vaccine, Work Packages (WP) 6.1 – 6.16. The COVID-19 Vaccine Work Packages 6.1 – 6.10 and 6.13 – 6.16 as described in the Exhibit-A, Statement of Work are considered added and funded non-severable independent work packages as of the date of this amendment; Work Packages 6.11 (Pediatric Study) and 6.12 (High-risk Populations are identified as Options to be exercised at a future date based on (i) JOC recommendation, (ii) availability of funding and (iii) a signed amendment between the Parties.

vii. updates the Essential Considerations in paragraph II.C. below;

viii. Article IV: Management of the Project, Section A (3) Organizational Chart, is updated to include the respective Technical Leads for the COVID-19 program;

ix. Within Agreement Number HHSO100201700018C, Article XIII: Subcontracting is amended to add a supplement section for COVID-19 initiatives; and

x. Within Agreement Number HHSO100201700018C, Article XVI: Special Clauses the Section R, Public Readiness and Emergency Preparedness Act ("PREP ACT") Coverage, is added.

II. AMENDMENTS TO AGREEMENT

A. Incorporate new Cost Share Estimates/Budget Summary and Budget Allocation/Workplan Structure (Exhibit B) to reflect the COVID-19 Vaccine estimated costs and cost shares.

1) Pursuant to Agreement Article VI(C), the budget allocation summary of assets is hereby replaced to incorporate the following.

M0008 Cost Share Estimates/Budget Summary

Summary	Invoiced 8/15/2017 Through 12/31/2018	1/1/2019 Through 12/31/2019	1/1/2020 Through 12/31/2020	1/1/2021 Through 12/31/2021	1/1/2022 Through 12/31/2022	1/1/2023 Through 12/31/2023	1/1/2024 Through 12/31/2024	Total
(b) (4) (BARDA:Janssen) Cost Share		Period 1	Period 2	Period 3	Period 4			
(b) (4)								
(b) (4) (BARDA:Janssen) Cost Share								
COVID-19 Vaccines discovery - Phase 3 Clinical Trial	(b) (4)							
(b) (4)								
Total	(b) (4)							
BARDA funding								
Janssen funding								

2) Budget Allocation/Workplan Structure (also included as Exhibit B) reflects the budget allocation summary and provides details for the budget incorporated in this Amendment 0008. This updated Exhibit B reflects the adjusted WPs 6.1 – 6.7 cost estimates, adds the new WPs (6.8 - 6.16) and replenishes funding (b) (4)

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(b) (4)

2019-nCoV Vaccines - New Asset added with Amendment 0006										
WP 6.1	WP 6.1 (CLIN 0001) Antigen design, manufacturability testing and preMVS manufacturing									
WP 6.2	WP 6.2 (CLIN 0002) Pre-Clinical Immunology									
WP 6.3	WP 6.3 (CLIN 0003) CMC Development until First in Human ("FIH")									
WP 6.4	WP 6.4 (CLIN 0004): Clinical Development and Regulatory Activities to Start First in Human Study									
WP 6.5	WP 6.5 (CLIN 0005) GLP Toxicology									
WP 6.6	WP 6.6 (CLIN 0006) GMP Manufacturing to Enable Clinical Trials									
WP 6.7	WP 6.7 (CLIN 0007) Phase 1/2a Clinical Trial									
WP 6.8	WP 6.8 (CLIN 0008) CMC Development and GMP Manufacturing Process to Enable Large Scale Manufacturing and Launch to Support the Regulatory Filing									
WP 6.9	WP 6.9 (CLIN 0009) Toxicology Studies									
WP 6.10	WP 6.10 (CLIN 0010) Phase 3 Study Adults									
WP 6.13	WP 6.13 (CLIN 0013) Other Clinical Studies									
WP 6.14	WP 6.14 (CLIN 0014) Regulatory Support									
WP 6.15	WP 6.15 (CLIN 0015) Project Management Support									
WP 6.16	WP 6.16 (CLIN 0016) Dissecting the Evolution of SARS-CoV-2 and Specific Humoral and Cellular Immunity Following Infection									
WP 6.11	**OPTION** - WP 6.11 (CLIN 0011) Pediatric Study									
WP 6.12	**OPTION** - WP 6.12 (CLIN 0012) High-risk Populations									
TOTAL										

(b) (4)

(b) (4)

B. Updated the Statement of Work - The Statement of Work shall be replaced to reflect the new COVID-19 Vaccine, Work Packages (WP) 6.1 – 6.16. The updated SOW for incorporation in the OTA is included in Exhibit A.

C. Essential Considerations as added via Amendment 0006 and amended herein and made applicable to Amendments 0007 (COVID-19 Antiviral) and 0008 (COVID-19 Vaccines):

By the Parties' mutual agreement and within the existing Agreement's general scope, this Amendment No. 0008 bilaterally acknowledges the Parties' agreement that:

i. Recipient will adhere to commercial practices when engaging subcontractors, including, if necessary, relief from OTA flow down provisions that otherwise may apply;

ii. Recipient will use reasonable efforts to include rights for BARDA consistent with its IP rights specified under Articles IX and X of the OTA in negotiations with third parties controlling such IP rights. In the circumstance that 1) a sub-contractor is not willing to agree to the flow-down terms regarding IP and data rights in Articles IX and X of the Flu OTA, and 2) the sub-contractor's proposed terms are materially less than the scope of the flow-down IP and data rights in Articles IX and X of the Flu OTA, then Recipient will confer with BARDA (OTAO, OTTR, and Respective Asset Lead) in writing (email is acceptable) to gain alignment on the sub-contractor IP and data rights that BARDA believes are necessary in the specific instance. Such alignment on BARDA's concerns with Recipient's sub-contractor's IP and data rights shall be provided within a reasonable timeframe based upon the urgency of the situation at that time. If alignment on sub-contractor IP and data rights reaches an impasse and BARDA is unable to accept any lesser rights than those for which it is entitled to under the Flu OTA, Recipient and BARDA agree that no government funds shall be used for the impacted scope of work, however, Recipient may proceed at its own cost. Such activities conducted at Recipient's own cost are not subject to the terms and conditions of this OTA; however, any impacted deliverables will be aligned to ensure program continuity;

iii. BARDA shall not restrict Recipient's engagement or collaboration with other parties, such as other agencies, international organizations, governments or NGOs, seeking Recipient's participation in the effort to develop solutions to counter the threat of the coronavirus, including receipt of funding (to the extent that Recipient is not receiving funding from multiple sources for the exact same work it is performing here under), use of Recipient's technology, or any other support or collaboration that Recipient determines is needed; and

iv. Reporting Requirements of the above referenced OTAs will include only those requirements necessary to maintain sufficient updating during these dramatically accelerated development programs.

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D. Article IV: Management of the Project Section A (3) Organizational Chart is deleted and replaced with the following:

(b)(4), (b) (6)

[redacted]

E. Article XIII: Subcontracting is amended to add a supplemental section for COVID-19 initiatives;

ARTICLE XIII: SUBCONTRACTING:

For this Amendment 0008 (Vaccines) and Amendment 0007 (Antiviral) only, for any subcontracts (b) (4) [redacted], that will be reimbursed under Amendment 0008 or Amendment 0007, Recipient will provide BARDA the opportunity to review the subject subcontracting agreement three (3) calendar days before execution. The subcontract agreement shall include the nature of the work that the subcontractor is going to perform, an estimated period of performance and the proposed costs for the work. Recipient will provide OTTR, OTAO and OTTS with an electronic copy of the subcontracting document. For avoidance of doubt, the Recipient is not required to wait for the Government's comments before executing an Agreement with a subcontractor once the 3-calendar day review period has expired.

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F. Article XVI: Special Clauses the following clauses are added:

i. Section R, Public Readiness and Emergency Preparedness Act ("PREP ACT") Coverage, is added:

R. Public Readiness and Emergency Preparedness Act ("PREP ACT") Coverage

The Federal Government may not use, or authorize the use of, any products or materials provided under either this agreement or any future purchase from Recipient's domestic manufacturing capacity unless such use occurs in the United States and is protected from liability under a declaration issued under the Public Readiness and Emergency Preparedness Act, 42 U.S.C. § 247d-6d.

Except as provided in this Amendment, all terms and conditions of the Agreement, unless previously changed, remain unchanged and in full force and effect.

III. SIGNATURES

Acknowledged, accepted, and agreed for

(b) (6)	U.S. Department of Health & Human Services
	Office of the Assistant Secretary for Preparedness & Response
	Biomedical Advanced Research & Development Authority
	BY: James Harris -S Digitally signed by James Harris -S Date: 2020.03.27 16:47:10 -04'00'
	NAME: James Harris
	ITS: Other Transaction Agreement Officer
DATE: 3/27/20	DATE:

ATTACHMENT 1: TASK DESCRIPTION DOCUMENT (SOW)

Overall Objectives and Scope

Seasonal and pandemic influenza remains one of the most important public health threats despite current vaccine and therapeutic options. The Consortium is developing a broad portfolio of innovative and novel countermeasures against influenza and other emerging infectious diseases comprising small molecules, biologics and vaccines. The portfolio employs (b) (modes of action complementary to current Standard of Care treatments to develop single or combination therapies that have the potential to increase therapeutic benefit and preclude the rapid emergence of drug resistance. The (b) (4) aims to (b) (4) the influenza vaccine field by providing broad protection for both seasonal and pandemic influenza.

Specifically, this Agreement includes: an influenza (b) (4) that is now ready for (b) (4) ; (b) (4) influenza A or B viruses; (b) (4) ; and (b) (4)

In addition, Recipient may propose to augment the portfolio by replacing molecules listed in this SOW with backup molecules from their ongoing research programs. With support from the JOC, the Consortium may also consider in-licensing drug or vaccine candidates to supplement the Program's portfolio of emerging infectious disease medical countermeasures in the Field. Recipient may also add Consortium Members as may be appropriate or complimentary to the performance and goals of this Agreement.

(b) (4)

(b) (4)

[redacted]

(b) (4)

[redacted]

6 Novel Coronavirus ("2019-nCoV") Vaccine

6.1 Antigen design, manufacturability testing and preMVS manufacturing

Activities

- DNA encoding for several designs of the SARS-CoV-2 spike protein will be ordered at multiple CROs
- Research batches of Ad26 vectors with transgenes that encode for the different designs of the spike protein will be produced
- A small-scale manufacturability test will be done to determine platform fit of the different Ad26-based vaccine candidate expressing the different designs of the spike protein.
- (b) (4)
  [redacted]
- The PreMVS, with selected antigen, will be released based on the following assays:

(b) (4)

[redacted]

- Several critical reagents such as expression plasmids, soluble proteins, peptide pools and detection antibodies will be generated or ordered

Milestones

- Selection of Ad26-based COVID-19 vaccine candidate for start of preMVS manufacturing
- Transfer of preMVS to development organization
- Release of preMVS (Triggers WP6.7)

Deliverables

- (b) (4) [redacted]
- PreMVS CoA
- PreMVS manufacturing report

Go/No go decisions

- Outcome of (b) (4) [redacted] and immunogenicity assessment triggers a "go" for preMVS manufacturing and start of CMC method development and GMP manufacturing preparations
- Selection of Ad26-based COVID-19 vaccine candidate for start of preMVS manufacturing (Triggers WP6.6)

WP6.2 Pre-Clinical Immunology (Performed at Janssen or BIDMC)

Activities

- Mice, (b) (4) [redacted] and non-human primates (NHP) will be immunized with DNA constructs of candidate vaccine inserts to set up immunogenicity assays and to get a first idea of immunogenicity.
- Ad26-based candidate vaccines will be tested for immunogenicity (b) (4) [redacted] mouse (b) (4) [redacted] Syrian hamster, (b) (4) [redacted] and NHP.
- Mice, Syrian hamster, rabbits, (b) (4) [redacted] and NHP will be considered for viral challenge studies. If challenge models can be developed, animals from immunogenicity studies with Ad26-based vaccine candidates may be rolled over to a challenge study to determine preclinical vaccine efficacy.
- The existence and relevance of vaccine-induced enhanced disease will be assessed in pre-clinical immunogenicity and relevant viral challenge models if available. (b) (4) [redacted]

Milestones

- Initial PoC based on immunogenicity of DNA vaccine constructs
- PoC based on immunogenicity of Ad26-based vaccine candidates

- PoC based on protective efficacy of Ad26-based vaccine candidate if a suitable challenge model can be established.

Deliverables

- Study reports of in vivo studies

Go/No go decisions

- Proof of immunogenicity triggers go for preMVS manufacturing

WP6.3 CMC Development until First in Human ("FIH")

Activities

- Previously generated AdVac® platform data and prior experience will be leveraged as much as possible from a manufacturing development. To de-risk the R&D program we are planning to perform one or two DS development runs.
- (b) (4) method development will occur to make insert specific assays fit for purpose.
- (b) (4) PER.C6® (b) (4) Ad26-based COVID-19 vaccine. (b) (4) PER.C6® cell line (b) (4) PER.C6® (b) (4)

(b) (4)

WP6.4 Clinical Development and Regulatory Activities to Start First in Human Study

Activities

- Setup of immunological assays at CROs or at Janssen:
  - VNA, ELISA, ICS and ELISpot
- Writing of protocol elements document (PED)
- Protocol writing
- Writing and submission of preIND document
- Writing and submission of IND documents
- Contracting with vendors

- Contracting with clinical sites

Milestones

- PreIND meeting
- IND open

Deliverables

- Development reports assays
- PED
- Clinical Protocol
- preIND briefing book
- preIND minutes
- IND
- Investigators Brochure

Go/No go decisions

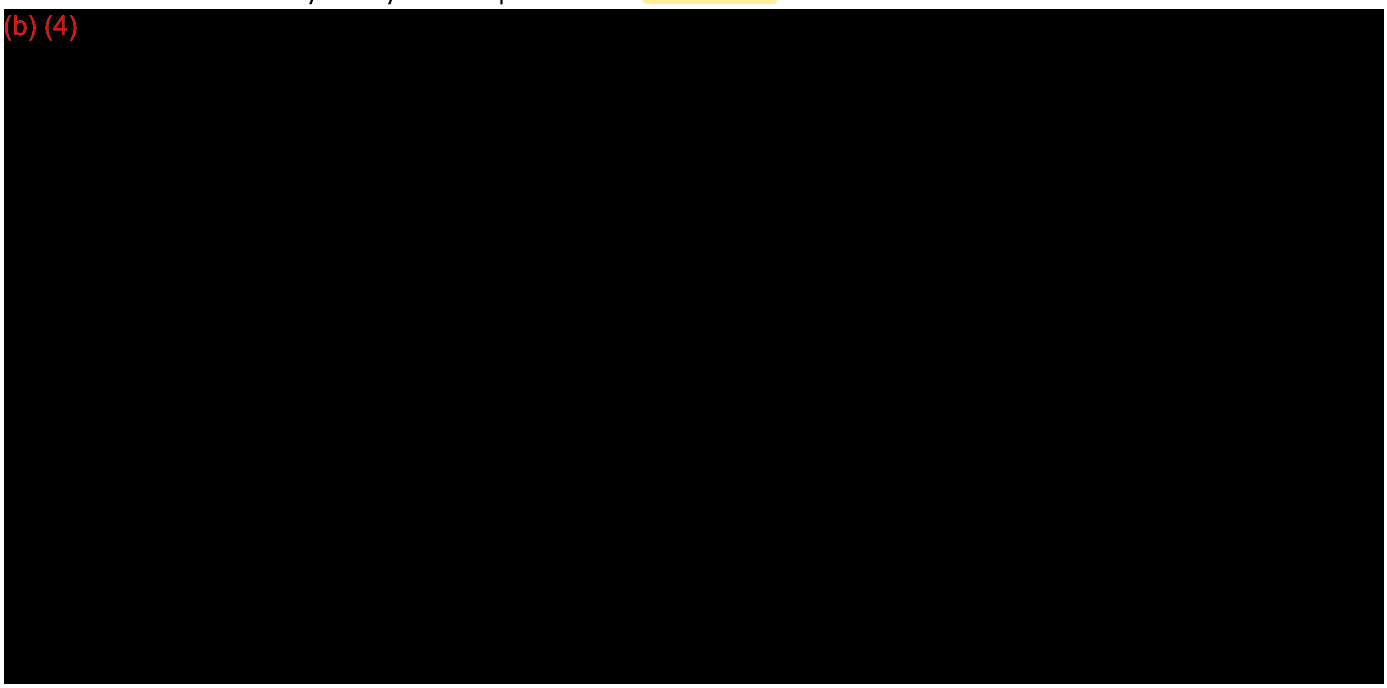
- preIND submission triggers start clinical trial (WP6.7)

WP6.5 GLP Toxicology

Activities

- A GLP Toxicity study will be performed in rabbits.

(b) (4)



WP6.6 GMP Manufacturing to Enable Clinical Trials

Activities until First in Human ("FIH")

- Master Virus Seed manufacturing and release

- Multiple drug substance batches will be manufactured (b) (4) [redacted]
- Drug Product manufacturing will happen (b) (4) [redacted]
- Packaging/labeling and distribution.
- Release and stability analysis will happen (b) (4) [redacted]

Activities for WPs 6.10 - 6.13,

(b) (4) [redacted]

WP6.7 Phase 1/2a Clinical Trial

Activities

- Randomized, placebo-controlled, (b) (4) [redacted], double blind study in healthy adult volunteers 18-55yrs, 65 and older.

- Primary objective will be assessment of safety and reactogenicity. Secondary and exploratory endpoints will evaluate vaccine-induced immune responses to SARS-CoV-2.
- Two dose levels (high dose and low dose) given intramuscularly, will be evaluated, either as a single immunization, or as two immunization regimens, and compared to placebo
- Th1/Th2 determination to characterize immune response; this is relevant in light of the unproven, yet, theoretical possibility of enhanced respiratory disease (ERD).
- Study will be divided into three cohorts: Cohort 1: 18-55 yr old, 5 groups, 4 active and one control group, 50 subjects/group; Cohort 2: 18-55 yr, 150 active and 50 controls for extension of safety data, collection of best regimen based on immunological data obtained in Cohort 1; Cohort 3 in 65 or older: similar design as Cohort 1. Cohorts 1& 2 total volunteers 450 subjects, Cohort 3. 250 subjects; Total study size 700 subjects.
- Serum and PBMC (PBMC in Cohorts 1 and 3, and a subset of Cohort 2) will be collected at day(s) of immunization, and at days 7, 14 and 28 after each immunization. Durability of immune responses will be measured at 6 months and after one year after last dose.
- Five subjects/group within Cohort 1 will be enrolled at BIDMC; samples will be subject to exploratory immune studies.

Milestones

- Interim analysis Cohort 1 after first dose for Safety and Immunogenicity to determine dose and if 1 dose is adequate to proceed to Cohort 2 for expanded safety. The decision to proceed to Cohort 2 is based on an algorithm related to immunological results. The decision to go to Cohort 3 is based upon the same algorithm used in decision to proceed from Cohort 1 to Cohort 2, in addition to any data from any required preclinical studies
- Primary Analysis Cohort 1 after 2nd dose for Safety and Immunogenicity to determine dose and if 2 doses are adequate to proceed to Cohort 2 expanded safety. This decision is based on an algorithm related to immunologic results. The decision to proceed to Cohort 3 is based on the same algorithm, in addition to any data from any required preclinical studies
- Decision to proceed to Phase 3 efficacy in aged 18-55 adults is based on Cohort 1 data.
- Primary analysis of Cohort 2 safety extension to confirm safety in enough individuals for Phase 3 efficacy.
- Final analysis top line results.

Deliverables

- TLR reports
- Clinical study report

Go/No go decisions

- Interim analysis Cohort 1 after 1 dose - Go/No go proceed to Cohort 2 and Phase 3 efficacy trial.
- Primary analysis Cohort 1 after 2 doses Go/No go proceed to Cohort 2 and Phase 3 (If decision cannot be reached after 1 dose).
- Primary analysis Cohort 2 to confirm safety decision to start Phase 3.

WP6.8 CMC Development and GMP Manufacturing Process to Enable Large Scale Manufacturing and Launch to Support the Regulatory Filing

(b) (4)

- PPQ for both DS and DP will be executed.

(b) (4)

- Studies to enable launch and support licensure will be assessed and executed as appropriate.

(b) (4)

(b) (4)

WP6.9 Toxicology Studies

A Phase 1 enabling GLP toxicology study is described under WP6.5. (b) (4)

Activities

- Conduct developmental and reproductive toxicity (DART) study

(b) (4)

WP6.10 Phase 3 Study Adults

A variety of factors including manufacturing and CMC considerations, preclinical data, the state of the COVID-19 pandemic and primarily the safety and the immunogenicity of the vaccine as demonstrated in Cohorts 1 & 2 of the Phase 1/2a study will be considered before proceeding to Phase 3 studies. (b) (4) [redacted]

The Phase 3 pivotal efficacy study, if necessary, will be a randomized placebo-controlled study in adults aged 18-55 to demonstrate protection against acquisition of PCR confirmed COVID-19. The sample size will vary based on the incidence and the primary endpoint of the trial and the lower bound of the 95% confidence interval of the point estimate of vaccine efficacy that regulatory agencies will accept. The sample size for a trial with an incidence of signs and symptoms of lower respiratory tract involvement of around 0.45/100 is around 25,000 subjects with a 1:1 ratio of vaccine to placebo. This is a conservative estimate of the incidence of LRTI for RSV infection in the elderly. Based on current epidemiology the incidence of COVID-19 appears to be higher than RSV incidence and the virus appears to be more infectious than influenza virus or RSV. In addition, the endpoint will be influenza-like illness which has a higher incidence than lower respiratory tract infections. A conservative estimate would be 12,500 participants. Incidence data as the pandemic evolves will give a better indication of sample size. (b) (4) [redacted]

(b) (4) [redacted]

Indication for protection against severe pneumonia, intubation and death will be dependent on incidence in the target population and may require post marketing or post utilization surveillance with a test negative design or other methodology.

Licensure for emergency use will depend on the state of the pandemic at the time clinical data is available and manufacturing readiness and CMC acceptance. The current plan is to acquire as much placebo-controlled randomized study data as possible.

International agencies are contemplating comparative trials between vaccine candidates and this will be considered at the time of proceeding to Phase 3.

OPTION - WP6.11 Pediatric Study

Clinical studies with immunologic endpoints will be performed in children (b) (4)
Sample size will be calculated (b) (4)

OPTION - WP6.12 High-risk Populations

(b) (4)

WP6.13 Other Clinical Studies

Phase 3 Consistency Lot Study

A Phase 3 consistency lot trial comparing (consecutive manufactured lots of the vaccine plus potentially a lot used in the Phase 3 efficacy trial (if consistency lot material is not utilized in the efficacy trial) will be performed. The objective of the study is to demonstrate that the immune responses to the (b) (4) lots are non-inferior to each other based on a margin acceptable to regulatory agencies. (b) (4)

Phase 3 End Expiry Study

A Phase 3 end expiry study will be performed to determine that the vaccine at the end of the shelf life is still immunogenic at a level that it elicits immune responses that are expected to be protective. (b) (4) The vaccine will then be tested at a dose that is consistent with this model for the end of shelf life, taking assay variation and stability into account. (b) (4)

(b) (4) [redacted]

Phase 3 Concomitant Use Trial

Phase 3 concomitant use trials may be performed. (b) (4) [redacted]

WP6.14 Regulatory Support

Activities to establish an IND for an Ad26-based COVID-19 vaccine will involve an arrangement of a pre-IND meeting with CBER before the intended IND submission (b) (4) [redacted]. Prior to the pre-IND, Janssen will discuss critical developmental aspects in Technical Working Group meeting(s) with FDA. Hence, throughout the program, RA CMC, Global Regulatory Affairs (RA) and regional RA support will be needed by preparing the respective working group meetings and providing regulatory advice internally within the Company.

As both pre-IND, IND and subsequent regulatory documentation will be supported by platform data both from a PER.C6® cell line perspective as the Ad26 vector, as well as use of non-clinical and clinical safety data from other developmental vaccines from Janssen, this platform information will need to be written down to be shared with the Agency. This activity will be coordinated by RA with support of the relevant CMC, non-clinical and clinical experts in the Company.

The pre-IND and IND preparation to enable Phase 1 will be led by RA. Further regulatory activities beyond Phase I are interactions with FDA to support the development of the vaccine up to regulatory submission (to be discussed: pre-EUA and/or BLA submission, or other pathways as per Agency's guidance). This involves an end-of-Phase 2 meeting and a pre-BLA meeting. Type C meetings will be scheduled on an as-needed basis. Pediatric requirements will be discussed as per Agency's requirements.

Annual reports will be prepared and submitted to CBER according to the foreseen timelines after the IND comes into effect. Development of regulatory intelligence with respect to development and licensing of a COVID-19 vaccine will carefully be monitored.

Discussions with other regulatory Agencies as required by the program and in particular to allow for a harmonized approach from a CMC, non-clinical and clinical development perspective, and facilitate multi-country trials as required per discussion with the Agencies, may also have to be conducted and will then be covered under WP6.14.

WP6.15 Project Management Support

This WP includes the Program Management activities associated with development of an Ad26-based COVID-19 vaccine. The program will have an Asset Project Management Leader (Asset PML) who will oversee their specific Project Management requirements. This includes conducting frequent and regular Project Management Team (PMT) meetings to ensure the accurate developing and tracking of the budget, timeline and resource plan. The Project Management team of each asset will also include relevant functional Project Managers and a Finance Representative. The Program will also have an Asset Technical Lead (CDT-L) who will oversee their specific Technical requirements. This includes conducting frequent and regular Compound Development Team (CDT) meetings to define the overall development strategy. The CDT of each asset will include, but is not limited to, the Technical Lead, Preclinical Leader, Clinical Leader, the CMC Leader and, the Regulatory Leader. Clinical Team and Trial teams will oversee clinical program and trial execution. These teams include operational staff, Operational Leader sand representatives of operational departments such as data management; GCO; medical writing, programming, stats. Additional expertise required for executing asset-specific work possibly including subcontractors may be added as part of PMT and CDT.

WP6.16 Dissecting the Evolution of SARS-CoV-2 and Specific Humoral and Cellular Immunity Following Infection

Activities

- The understanding of the roles that polyclonal antibody responses to SARS-CoV-2 are thought to play in protection, disease resolution, or enhancement of disease are evolving with the assessment of patients with varying disease outcomes. The role of T cell responses is being investigated as well. Qualitative and quantitative characterization of immune responses upon SARS-Cov-2 infection, potentially in relation to outcome, could help to inform vaccine development.
- Identification of antigen-specific biomarkers of disease trajectory (survival, disease, death) and SARS-CoV-2 specific immune responses against the virus by (b) (4) approaches (b) (4) using samples from previously and prospectively collected, longitudinal cohorts at the (b) (4)

Milestones

- (b) (4) [redacted]
- Biophysical characterization of antigen-specific antibody responses by Fc-receptor Luminex array and glycosylation profiling (S and RBD proteins of SARS-CoV2, SARS1, MERS, and other respiratory viruses; Galit Alter, Massachusetts General Hospital, Boston, MA)
- Functional characterization of antigen-specific antibody responses using antibody-dependent cellular phagocytosis (ADCP), complement deposition (ADCD), neutrophil or dendritic cell phagocytosis (ADNP and ADDCP), NK-cell activation and cytotoxicity (ADNA and ADCC), ERD, and other ADxx assays (SARS-CoV-2 S antigen; Galit Alter, Massachusetts General Hospital, Boston, MA)

Deliverables

- Study reports

Go/ no-go: There are no Go/No go decisions linked to these characterizations

7 COVID-19 Antiviral Discovery and Clinical Development

Outlined below is the full development program for a typical hit from screening a library of compounds that have not been clinically tested in humans for any uses. Steps described below cover (b) (4) [redacted] Described activities are therefore subject to change upon data-driven decision.

In case a (b) (4) [redacted], the development program could be significantly accelerated. Depending on the availability of e.g. (b) (4) [redacted] upon joint decision.

WP 7.1 Continuation (b) (4) [redacted]

Depending on the nature of the identified (b) (4) [redacted], additional efforts may need to be undertaken to (b) (4) [redacted]

WP 7.2 Lead and Late Lead Optimization

The purpose of lead optimization (b) (4) and a go-no go decision will be taken whether or not to move to pre-clinical development.

WP 7.3 Pre-Clinical development

This phase includes studies in (b) (4). This may include, but not be limited to: (b) (4)

This phase will also include (b) (4) and Phase 1 clinical trials, including stability studies. It may also include pre-formulation for Phase 1 clinical trials.

Phase 1 first-in-human formulation development will follow (b) (4) (conditional to JOC approval). Based on the result of the formulation development work, clinical study materials packaging, labeling and distribution will start and clinical pharmacy manual of Phase 1 trial will be developed.

WP 7.4 Clinical development

WP 7.4.1 Clinical Phase 1

This stage includes a first-in-human clinical Phase 1 and may include additional supportive clinical Phase 1 studies as well.

7.4.2 Clinical Phase 2a Study

(b) (4), this stage may include a clinical Phase 2a study to investigate the therapeutic efficacy and safety of the drug in (b) (4). This Phase 2a study may or may not include (b) (4) depending on available data for the asset selected.

7.4.3 Clinical Phase 2b Study

Depending on the available data of the asset and the results of the Ph2a study, a confirmatory Ph2b study can be performed as a separate study, or in (b) (4).

This stage also includes further Drug Substance and Drug Product development for Phase 2 studies.

These (b) (4) will continue in the next phases:

- (b) (4)
- Registration and Validation phase

(b) (4)

WP 7.5 Regulatory

WP 7.5.1 Regulatory through to Phase 2b clinical study

Janssen intends to seek regulatory and scientific advice from the regulatory authorities throughout the development of the project, including the first occasion as pre-IND consultations with FDA, before submitting the IND with a phase 1 clinical study. During Phase 2 and onward this would include Type C meetings, and additional meetings to seek further guidance on our overall development program. Similar type Scientific Advice meetings in the EU are included. Depending on the epidemic status and continued unmet medical need, FDA accelerated approval and EMA conditional approval could be requested, based on Ph2 results.

WP 7.5.2 Regulatory from Phase 3 and registration

Janssen will continue to seek regulatory and scientific advice from the regulatory authorities throughout Phase 3 of the project. This includes but not limited to, discussing the Phase 3 clinical study designs and an overall proposed clinical data set in support of new or expanded licensure.

8 Project Management

(b) (4)

8.1 Joint Oversight Committee

The Joint Oversight Committee (JOC) is the larger decision-making body that provides guidance, direction and control to the projects to ensure execution of the projects according to the SOW. The JOC will discuss and approve any changes to the SOW. To that extent, the JOC will meet at critical decision points in the program, but no less than two times per year, preferably face to face or alternatively by WebEx or telephone conference. Ad hoc meetings will be organized when urgent matters arise. The JOC will consist of voting and non-voting members from BARDA and Janssen. Additional, non-voting members can be assigned or invited on an ad hoc basis. Decisions to reprioritize specific projects and resources as the need arises will be taken by consensus. In case such a decision cannot be

reached in the JOC, the decision will be escalated to one BARDA and one Janssen senior management member identified at the start of the project.

8.2 PMO Steering Committee

The PMO (Program Management Organization) steering committee has dual responsibilities. One area of responsibility is the communication and coordination with BARDA regarding day to day management and execution of the project e.g. organizing meetings on a regular agreed basis. In addition, the PMO Steering Committee will coordinate all SOW activities and provide the technical and administrative infrastructure to ensure efficient planning, initiation, implementation, direction, management and completion of all tasks. This will be coordinated by the Project Manager Leader (PML). The Steering Committee will assess progress and where needed will work out strategic changes to be decided upon by the JOC. The Steering Committee consists of a group of dedicated and specialized Project Management experts, key personnel and additional specific expertise for the functions that are required for executing the specific work scope for each proposed asset area.

8.3 Asset Project Management (WP 2.5, WP 5.5, WP 6.15, WP 7.6.1, and 7.6.2)

These WPs include the Program Management activities associated with each of the assets. Each asset will have an Asset Project Management Leader (Asset PML) who will oversee their specific Project Management requirements. This includes conducting frequent and regular Project Management Team (PMT) meetings to ensure the accurate developing and tracking of the budget, timeline and resource plan. The Project Management team of each asset will also include relevant functional Project Managers and a Finance Representative. Each asset will also have an Asset Technical Lead who will oversee their specific Technical requirements. This includes conducting frequent and regular Compound Development Team (CDT) meetings to define the overall development strategy. The CDT of each asset will include Technical Lead, Preclinical Leader, Clinical Leader, the CMC Leader and, the Regulatory Leader. Additional expertise required for executing asset-specific work possibly including subcontractors may be added as part of PMT and CDT.

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[redacted] (b) (4)

2019-nCoV Vaccines - New Asset added with Amendment 0006	
WP 6.1	WP 6.1 (CLIN 0001) Antigen design, manufacturability testing and preMVS manufacturing
WP 6.2	WP 6.2 (CLIN 0002) Pre-Clinical Immunology
WP 6.3	WP 6.3 (CLIN 0003) CMC Development until First in Human ("FIH")
WP 6.4	WP 6.4 (CLIN 0004): Clinical Development and Regulatory Activities to Start First in Human Study
WP 6.5	WP 6.5 (CLIN 0005) GLP Toxicology
WP 6.6	WP 6.6 (CLIN 0006) GMP Manufacturing to Enable Clinical Trials
WP 6.7	WP 6.7 (CLIN 0007) Phase 1/2a Clinical Trial
WP 6.8	WP 6.8 (CLIN 0008) CMC Development and GMP Manufacturing Process to Enable Large Scale Manufacturing and Launch to Support the Regulatory Filing
WP 6.9	WP 6.9 (CLIN 0009) Toxicology Studies
WP 6.10	WP 6.10 (CLIN 0010) Phase 3 Study Adults
WP 6.13	WP 6.13 (CLIN 0013) Other Clinical Studies
WP 6.14	WP 6.14 (CLIN 0014) Regulatory Support
WP 6.15	WP 6.15 (CLIN 0015) Project Management Support
WP 6.16	WP 6.16 (CLIN 0016) Dissecting the Evolution of SARS-CoV-2 and Specific Humoral and Cellular Immunity Following Infection
WP 6.11	**OPTION** - WP 6.11 (CLIN 0011) Pediatric Study
WP 6.12	**OPTION** - WP 6.12 (CLIN 0012) High-risk Populations
TOTAL	

[redacted] (b) (4)

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